

Incidence of Treated Snakebites in the United States

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SNAKEBITE ACCIDENTS happen more frequently in the United States than most people realize. Recent estimates (1) of about 1,000 to 2,000 such accidents annually have been far too low. There have been surprisingly few studies of the magnitude of the incidence. Willson (2) in 1908 reviewed 740 snakebite cases spanning several years; data on 440 of these were collected from reviewing the literature; information on the remainder was assembled from various private sources. Hutchison (3,4) described 607 case reports of snake venom poisonings in the United States occurring during 1928 and 482 reports of poisonings occurring during 1929. These case histories were obtained from newspaper clippings and report forms distributed in packages of antivenin. Since antivenin was not widely used or distributed in this country before 1928, Hutchison's study probably underestimated the incidence of poisonous snakebites. By similar methods, Githens (5) collected information on 2,376 cases of snakebite which occurred in the United States from 1927 through 1934. Thus, before the present study there never had been a systematic, nationwide study of snakebite accidents.

Poisonous Snakes

Of the species of snakes native to the United States, only about 10 percent are poisonous (6). Snakes of the family Crotalidae (pit vipers) comprise the bulk of these venomous species. Pit vipers native to the United States comprise: *Crotalus*, or large rattlesnakes, *Sistrurus*, or

pigmy rattlesnakes, and *Ancistrodon*, or moccasins—including copperheads and cottonmouths. Coral snakes (of the genera *Micrurus* and *Micruroides*) are the only other native poisonous snakes. One or more species of poisonous snakes is found in every State except Alaska, Hawaii, and Maine (fig. 1).

Pit vipers have a characteristic pit located between the eye and the nostril on each side of their bodies. They also are identified by elliptical pupils and two well-developed fangs which protrude from their maxillae when their mouths are opened. Rattlesnakes have rattles attached to their tails. Harmless snakes have no facial pits and have round rather than elliptical pupils; while they have teeth, they lack fangs.

Often a person will chop off the head of a snake that has bitten someone and bring the snake's body in for identification. Pit vipers can be identified by turning the snake's belly upwards and noting a single row of subcaudal plates just below the anal plate. Harmless snakes have a double row of subcaudal plates. Figure 2 depicts the characteristic features of pit vipers and of harmless snakes.

The coral snake is a small, beautifully colored reptile with broad rings of scarlet and black separated by narrow rings of yellow—"red next to yellow will kill a fellow." The snout is always black. Several harmless snakes resemble coral snakes, but the yellow and red rings on their bodies are separated by black rings. Coral snakes have round pupils and lack facial pits.

Methods of Study

The questionnaire and letter explaining the purpose of this study were mailed to a selected group of United States hospitals listed in the

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guide issue of *Hospitals*, journal of the American Hospital Association. All States except Alaska and Hawaii were included in the survey. The medical facilities selected were general hospitals, children's hospitals, and college infirmaries. Army, Navy, Coast Guard, Public Health Service, Air Force, and Veterans Administration hospitals also were sent questionnaires. Maternity, tuberculosis, and mental hospitals were omitted since they would not be expected to treat snakebite victims. Each hospital was requested to report all inpatients admitted for treatment of poisonous snakebite during 1958 and 1959 and all such treatment given. Second, third, and fourth followup letters were sent as necessary. Hospital inpatient reports for the 2 years were requested to determine if there was a large variation in snakebite cases from year to year.

Most hospitals do not code and tabulate diagnoses for patients visiting emergency rooms and outpatient clinics. Since some snakebite victims are not admitted to hospitals as inpatients, it seemed essential to ask a sample of practicing physicians how many snakebite victims they treated as outpatients—in an office, home, emergency room, and the like—and how many as inpatients.

Previous surveys (7,8) have shown that general practitioners, surgeons, internists, pediatricians, and orthopedic surgeons treat most people with venomous snakebites. Therefore a random sample of one-third of all physicians in these categories of practice who were listed in the American Medical Association's American Medical Directory were sent questionnaires.

Death certificates for fatal snakebite cases were obtained from State health departments.

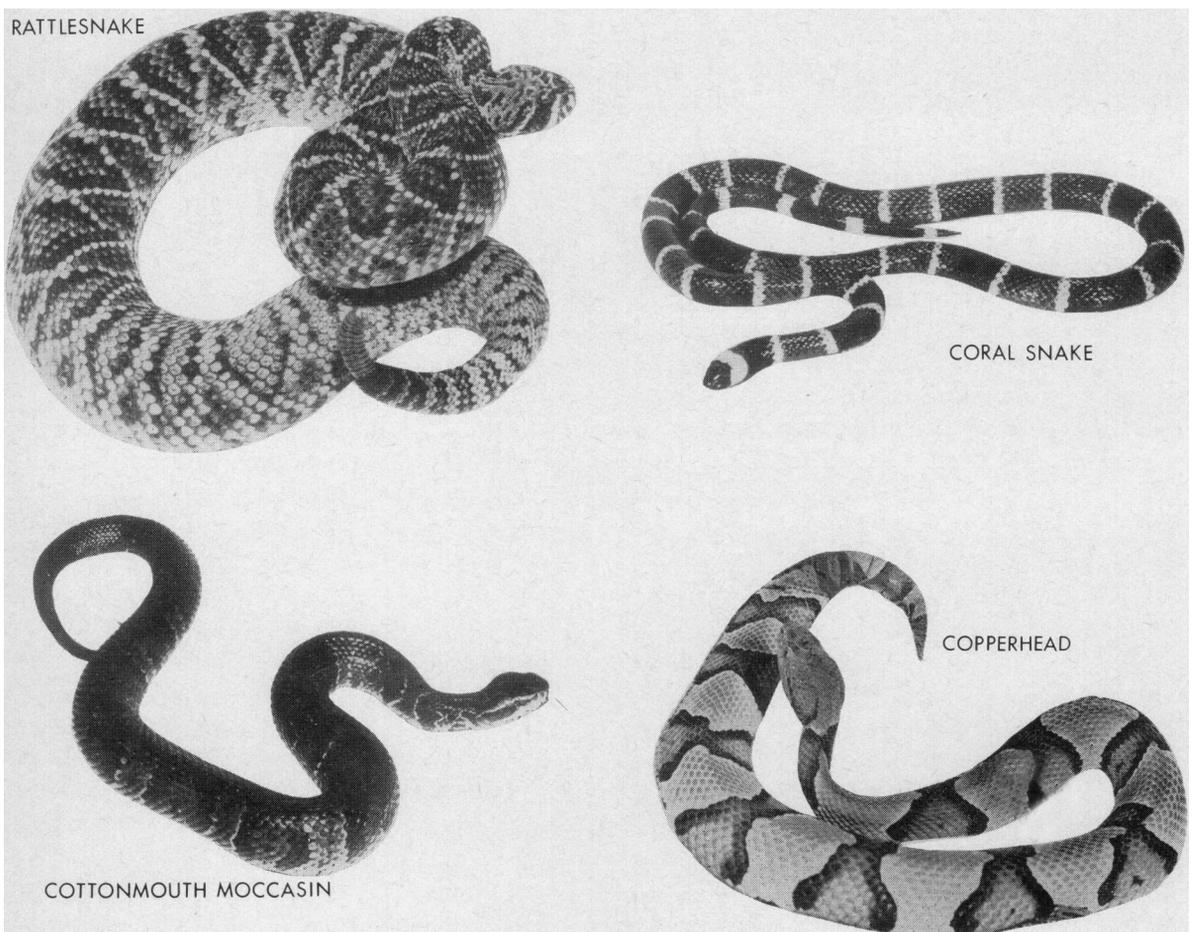


Figure 1. Poisonous snakes native to the United States

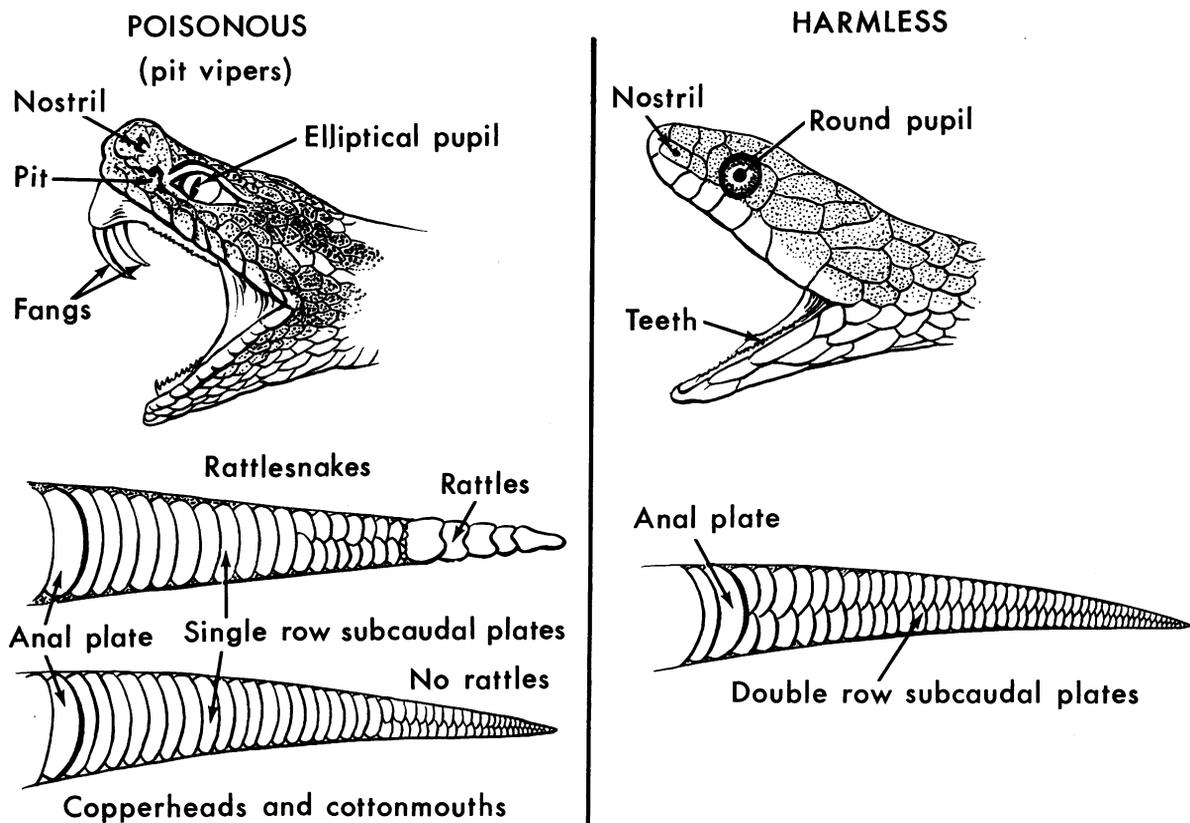


Figure 2. Characteristic features of poisonous snakes (pit vipers) and of harmless snakes

Results

This report is mainly based on data from questionnaires returned by 5,361 U.S. hospitals on poisonous snakebite treatments. All the analyses in the paper except the estimate of incidence are based on 2,836 detailed case reports received from the hospitals. Supplementary data, from questionnaires returned by 27,309 practicing physicians in the United States are used only in the estimate of incidence. Each State health department reported total fatalities in 1958 and 1959.

Of the 5,535 hospitals that were sent questionnaires, 96.9 percent returned them. Hospitals in 24 States provided 100 percent reporting. In the State with the lowest response, 85 percent of the hospitals participated. Of the 36,627 practicing physicians who were sent questionnaires, 74.6 percent returned them. The range of responses from physicians in the various States was from 66 to 88 percent.

Incidence. The hospitals surveyed reported a

total of 3,367 inpatients treated for poisonous snakebites during 1958 and 1959. There were 1,555 cases in 1958 and 1,812 in 1959—an average of 1,683.5 cases per year. Of the 3,367 inpatients that the hospitals reported were treated for snakebites, detailed reports were received for 2,836; only the number of bites was reported for the other 531.

The physicians' reports on snakebite accidents, when adjusted to account for all physicians in the practice categories represented, indicated that approximately 3,603 inpatients and 3,075 outpatients were treated for snakebite accidents annually. Careful analysis of these data by State showed that the difference between the estimate of 3,603 inpatients reported by physicians and the average of 1,683.5 inpatients reported by hospitals could be explained for the most part by the following facts: (a) 174 hospitals did not participate in the study; (b) there was evidence of underreporting of snakebite inpatients from at least 234 hospitals which

participated in the study; (c) many counties from which physicians reported snakebites did not have hospitals listed in *Hospitals* guide issue; and (d) physicians reported that some inpatients were treated in small clinics and hospitals not listed in this issue.

State health departments reported 15 deaths resulting from snakebites in 1958 and 14 in 1959.

On the basis of all these various reports, I estimate that approximately 6,680 persons in the United States (excluding Alaska and Hawaii) were treated for poisonous snakebites during 1959. This estimate provides an incidence of 3.74 bites per 100,000 population per year. Since there were 14 fatal snakebites during 1959, the case-fatality rate was 0.21 percent. Using the 1960 census of the population (excluding Alaska and Hawaii) as the denominator and 6,680 snakebite cases as the numerator, the mortality rate from snakebites was 0.08 per million population. Thus, less than 1 person in 10 million died from snakebites annually.

The incidence of snakebite accidents per 100,000 population was estimated as 4.99 for white males, 5.87 for nonwhite males, 2.44 for white

Table 1. Estimated age distribution of snakebite victims in the United States (excluding Alaska and Hawaii), 1959

Age group (years)	Population at risk ¹	Estimated bites ²	Rate per 100,000
0-4	20,205,746	650	3.22
5-9	18,592,413	1,039	5.59
10-19	29,837,176	1,755	5.88
20-29	21,530,609	872	4.05
30-39	24,295,263	796	3.28
40-49	22,380,675	546	2.44
50-59	17,974,066	506	2.82
60-69	13,367,970	318	2.38
70 or more	10,280,318	146	1.42
Not stated		52	
Total	178,464,236	6,680	3.74

¹ Denominator for the rates based on the 1960 census of the population of the United States (excluding Alaska and Hawaii).

² Numerator for the rates estimated from a projection of the proportion of hospital inpatients in each age group.

females, and 2.48 for nonwhite females. Thus, males had higher bite rates than females, and nonwhites had higher rates than whites. This distribution of bites by sex held true in most

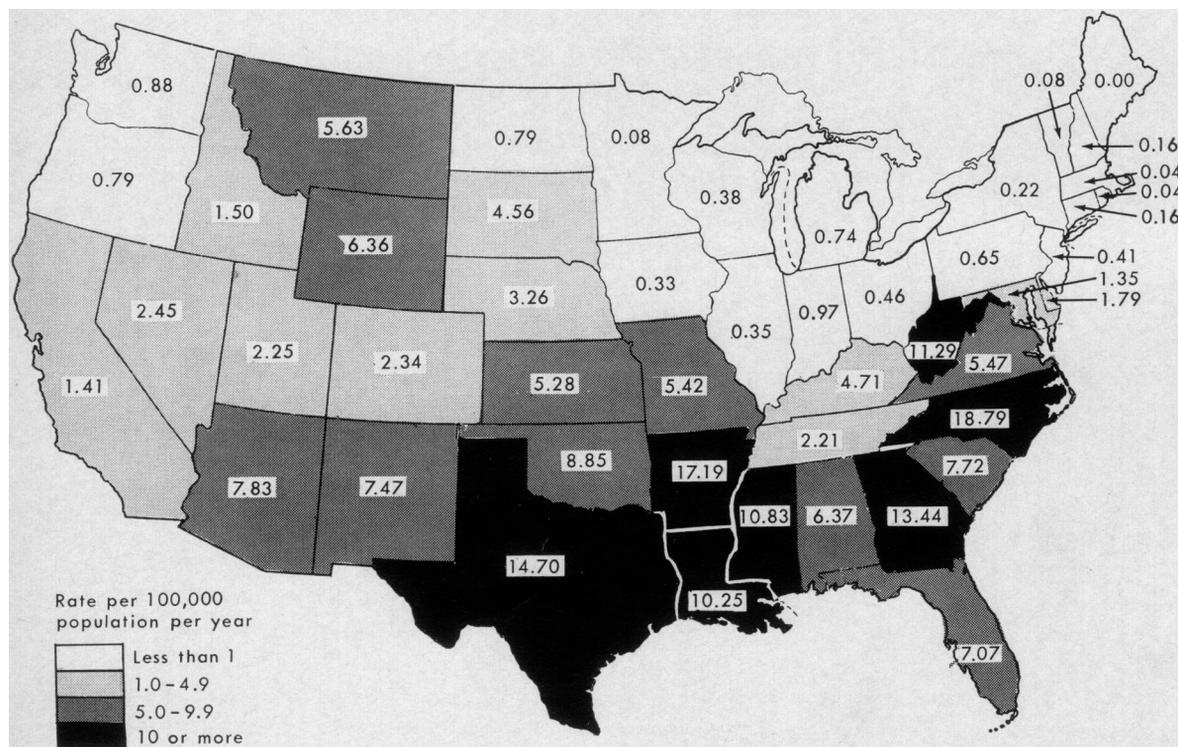


Figure 3. Geographic distribution of snakebite rates in the United States, 1959

States. Whites, however, had higher bite rates than nonwhites in most States. In approximately eight States where the reverse was true, the rates for nonwhites were excessively high and weighted the national average in favor of a higher bite rate for nonwhites.

Table 1 depicts the estimated age distribution of snakebite victims in the United States during 1959. Approximately 3,444 (52 percent) of the bites happened to persons less than 20 years of age. Age-specific bite rates are much more meaningful since they take into account the population at risk in a particular age group. The highest bite rates per 100,000 population were found in persons 10-19 years of age (5.88) and in those in the 5-9 age group (5.59). Children less than 5 years of age did not have an excessively high rate (3.22). The lowest bite rate was for persons 70 or more years of age (1.42).

Geopathology. The geographic distribution of poisonous snakebites is shown in figure 3. Most of the States having the highest bite rates per 100,000 population per year (darker shade on the figure) were in the southeast and southwest. The States east of the Mississippi River having the highest annual bite rates per 100,000 population were North Carolina 18.79, Georgia 13.44, West Virginia 11.29, Mississippi 10.83, and South Carolina 7.72. The States west of the Mississippi River having the highest rates were Arkansas 17.19, Texas 14.70, Louisiana 10.25, Oklahoma 8.85, and Arizona 7.83. Poisonous snakebites were reported from every State in the study group except Maine. The highest snakebite rates per 100,000 population per year were found in the following regions: West South Central 13.30, South Atlantic 9.25, East South Central 5.53, Mountain 4.52, and West North Central 2.88.

Table 2 lists the estimated number of victims of poisonous snakebites treated as outpatients and as inpatients for each State and region in the country. It may surprise many people that 3,075 (46 percent) of 6,678 snakebite victims were treated as outpatients. Many bites by poisonous snakes, however, produce either minimal venenation or no venenation at all.

Of 2,836 persons hospitalized for snakebite treatment for whom detailed records were available, 954 (33.6 percent) were bitten by rattle-

snakes, 811 (28.6 percent) by copperheads, 208 (7.3 percent) by cottonmouth moccasins, 11 (0.4 percent) by coral snakes, 7 (0.3 percent) by foreign venomous snakes, and 846 (29.8 percent) by unidentified poisonous snakes. The clinical findings of bites by unidentified snakes suggest that most of these bites were inflicted by pit vipers. The geographic pattern of bites by various kinds of snakes was consistent with the ecologic ranges of poisonous snakes in the United States described by Conant (9) and Klauber (1). The major exceptions to this pattern occurred when people were bitten by captive native and captive foreign snakes. For example, a captive cobra (*Naja naja*) bit a pet-shop worker in Missouri. Obviously, cobras are not native to Missouri. Similarly, a radio announcer was bitten in Colorado while handling a captive, non-native cottonmouth moccasin.

Temporal relationships. Based on the records of the 2,836 hospital inpatients treated for snakebite during 1958 and 1959, the distribution by month was as follows:

Month	Bites	Month	Bites
January	9	August	530
February	17	September	453
March	39	October	186
April	137	November	75
May	354	December	20
June	437	Not stated	17
July	562		

Snakebites were infrequent during the colder months of the year—November through March—when in general snakes are inactive or hibernating. Ninety-four percent of the bites happened from April through October. The peak months for snakebite accidents in the United States are July and August. This striking seasonal distribution of bites coincides with the period when snakes are most abundant and active and when people have greater exposure because of outdoor occupations and recreation.

The percentage of bites that happened during various 3-hour periods of the day were: 6:00-8:59 a.m.—8.9 percent, 9:00-11:59 a.m.—17.2 percent, 12:00 noon-2:59 p.m.—16.9 percent, 3:00-5:59 p.m.—23.2 percent, 6:00-8:59 p.m.—19.8 percent, 9:00-11:59 p.m.—5.6 percent, 12:00 midnight-2:59 a.m.—0.6 percent, 3:00-5:59 a.m.—0.4 percent, and time not stated—7.4 per-

Table 2. Estimated incidence of poisonous snakebites in the United States (excluding Alaska and Hawaii), by region and State, 1959

Region and State	Estimated cases			Incidence per 100,000 population per year ¹
	Inpatient	Outpatient	Total	
New England.....	7.6	0	7.6	0.07
Maine.....	0	0	0	0
New Hampshire.....	1.0	0	1.0	.16
Vermont ²3	0	.3	.08
Massachusetts.....	2.0	0	2.0	.04
Rhode Island ²3	0	.3	.04
Connecticut.....	4.0	0	4.0	.16
Middle Atlantic.....	57.0	79.0	136.0	.40
New York.....	12.0	25.0	37.0	.22
New Jersey.....	15.0	10.0	25.0	.41
Pennsylvania.....	30.0	44.0	74.0	.65
East North Central.....	88.0	110.0	198.0	.55
Ohio.....	24.0	21.0	45.0	.46
Indiana.....	20.0	25.0	45.0	.97
Illinois.....	11.0	24.0	35.0	.35
Michigan.....	26.0	32.0	58.0	.74
Wisconsin.....	7.0	8.0	15.0	.38
West North Central.....	215.0	228.0	443.0	2.88
Minnesota.....	3.0	0.0	3.0	.09
Iowa.....	6.0	3.0	9.0	.33
Missouri.....	111.0	123.0	234.0	5.42
North Dakota.....	5.0	0.0	5.0	.79
South Dakota.....	22.0	9.0	31.0	4.56
Nebraska.....	20.0	26.0	46.0	3.26
Kansas.....	48.0	67.0	115.0	5.28
South Atlantic.....	1,255.0	1,147.0	2,402.0	9.25
Florida.....	209.0	141.0	350.0	7.07
Georgia.....	304.0	226.0	530.0	13.44
South Carolina.....	104.0	80.0	184.0	7.72
North Carolina.....	392.0	464.0	856.0	18.79
Virginia.....	112.0	105.0	217.0	5.47
West Virginia.....	111.0	99.0	210.0	11.29
Maryland.....	18.0	24.0	42.0	1.35
Delaware.....	2.0	6.0	8.0	1.79
District of Columbia.....	3.0	2.0	5.0	.65
East South Central.....	356.0	310.0	666.0	5.53
Tennessee.....	43.0	36.0	79.0	2.21
Kentucky.....	92.0	51.0	143.0	4.71
Alabama.....	108.0	100.0	208.0	6.37
Mississippi.....	113.0	123.0	236.0	10.83
West South Central.....	1,251.0	1,004.0	2,255.0	13.30
Arkansas.....	152.0	155.0	307.0	17.19
Louisiana.....	195.0	139.0	334.0	10.25
Oklahoma.....	120.0	86.0	206.0	8.85
Texas.....	784.0	624.0	1,408.0	14.70
Mountain.....	210.0	100.0	310.0	4.52
Montana.....	18.0	20.0	38.0	5.63
Idaho.....	6.0	4.0	10.0	1.50
Wyoming.....	12.0	9.0	21.0	6.36
Colorado.....	30.0	11.0	41.0	2.34
New Mexico.....	59.0	12.0	71.0	7.47
Arizona.....	72.0	30.0	102.0	7.83
Utah.....	9.0	11.0	20.0	2.25
Nevada.....	4.0	3.0	7.0	2.45
Pacific.....	163.0	97.0	260.0	1.28
Washington.....	20.0	5.0	25.0	.88
Oregon.....	5.0	9.0	14.0	.79
California.....	138.0	83.0	221.0	1.41

¹ The numerator for this rate is based on the estimated number of snakebites occurring during 1959. The denominator is based on the 1960 census of the population of the United States.

² There was approximately one poisonous snakebite every 3 years in Vermont and Rhode Island.

cent. Thus, the majority of snakebite accidents happen between 6:00 a.m. and 8:59 p.m., which is the period when people are most active outdoors. Many species of poisonous snakes are nocturnal feeders, but people, particularly children, simply do not have as much exposure to the possibility of a bite during the hours after dark.

Site and severity. Most of the poisonous snakebites were inflicted on the person's extremities (table 3.) The anatomical site of 38 percent was the upper extremities and of 58 percent, the lower. On the upper extremities, the hands and fingers were the parts most often bitten. The lower leg, including the ankle and the foot, was the part most frequently bitten on the lower extremities. About 0.5 percent of the bites were inflicted on the head, face, and neck and 0.7 percent on the trunk of the body. For 2.8 percent of the bites, the site was not stated. It is interesting that the right side of the body was bitten more frequently than the left side (55 percent compared with 42). The side bitten was not reported in 3 percent of the cases.

A modification of the clinical classification of pit viper venenation by Wood and associates (10) was used to determine the severity of bites. Bites were classified as follows:

Table 3. Anatomical sites of bites inflicted by poisonous snakes on persons in the United States (excluding Alaska and Hawaii), 1958-59

Anatomical site	Right side	Left side	Both sides	
			Number	Percent of total bites
Head, face, and neck	9	6	15	0.5
Trunk, front	2	6	8	.3
Trunk, back	9	3	12	.4
Upper arm	12	8	20	.7
Forearm	64	57	121	4.3
Hand	197	126	323	11.4
Fingers	377	224	601	21.2
Upper leg	32	29	61	2.2
Lower leg and ankle	407	340	747	26.3
Foot	386	320	706	24.9
Toes	78	64	142	5.0
Not stated			80	2.8

Grade 0—No venenation. Fang or tooth marks, minimal pain, less than 1 inch of surrounding edema and erythema. No systemic involvement.

Grade 1—Minimal venenation. Fang or tooth marks, severe pain, 1-5 inches of surrounding edema and erythema in first 12 hours after bite. Usually no systemic involvement.

Grade 2—Moderate venenation. Fang or tooth marks, severe pain, 6-12 inches of surrounding edema and erythema. Systemic involvement may be present—nausea, vomiting, giddiness, shock, or neurotoxic symptoms.

Grade 3—Severe venenation. Fang or tooth marks, severe pain, more than 12 inches of surrounding edema and erythema in first 12 hours after bite. Systemic involvement usually present as in grade 2.

The severity of venenation (venom poisoning) was classified for 2,433 hospitalized patients as follows:

Grade	Number	Percent
0	667	27
1	892	37
2	527	22
3	347	14

For the remaining 403 hospitalized patients, severity of venenation was not stated. Paradoxically, 27 percent of bites by poisonous snakes resulted in no signs of venom poisoning. This phenomenon has been documented by several investigators (1,7,10,11). Even more surprising, 64 percent (grade 0 and grade 1) of the bites were not life threatening. This finding helps dispel the popular notion that every bite by a poisonous snake is severe and will terminate fatally without treatment. The finding should thus be reassuring to physicians who treat snakebites. Nevertheless, a person bitten by a poisonous snake should not let this statistic stop him from seeking prompt medical diagnosis and treatment.

Summary

The incidence of treated poisonous snakebites in the United States (excluding Alaska and Hawaii) was determined by using hospital records, physician reports, and death certificates. An estimated 6,680 persons were treated for poisonous snakebites during 1959, an incidence of 3.74 bites per 100,000 popula-

tion. The case-fatality rate was 0.21 percent. Males had higher bite rates than females, and nonwhites had higher rates than whites. Fifty-two percent of the bites happened to persons less than 20 years of age. Regions having the highest bite rates per 100,000 population were the West South Central, South Atlantic, and East South Central. July and August were the peak months for snakebite accidents. Most of the bites were inflicted on the victims' extremities—38 percent on the upper extremities and 58 percent on the lower.

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Azulene Analogs of Pharmacologic Agents



Investigation of the pharmacodynamic activity of azulene and azulene derivatives, principally hydrocarbons, has been restricted primarily to examining the antiphlogistic, antiallergic, and bacteriostatic properties of these compounds or mixtures of them obtained from chamomile and similar oils.

This study was devoted to examining the effects of replacing benzenoid nuclei in structures known to exhibit pharmacologic activity with the nonbenzenoid aromatic nucleus of azulene.

Because the aromatic portions of local anesthetics are essential to a high level of local anesthetic activity, several azulene compounds were prepared which might be expected to be local anesthetics were their aromatic portions benzenoid rather than nonbenzenoid.

The compounds, a series of esters of azulene-1-carboxylic acid, some of which showed local anesthetic activity, were prepared by the room-temperature chlorocarboxylation of azulene in toluene with phosgene and reaction of the resulting acid chloride in situ with an appropriate

alkanol, haloalkanol, or aminoalkanol. The series was extended by reaction of the thus formed haloesters with a secondary amine or by ring nitration of a haloester with cupric nitrate in acetic acid and subsequent reaction of the nitrohaloester with a secondary amine followed by reduction to an aminoalkanol ester of an aminoazulene-1-carboxylic acid.

The new compounds prepared in this series include: 2-chlorethyl ester of azulene-1-carboxylic acid, 2-dimethylaminoethyl ester of azulene-1-carboxylic acid, 2-diethylaminoethyl ester of azulene-1-carboxylic acid, 2-(2-methyl)-piperidinoethyl ester of azulene-1-carboxylic acid, N-cyclohexyl-2-aminopropyl ester of azulene-1-carboxylic acid, 2-chloroethyl ester of 3-nitroazulene-1-carboxylic acid, 2-diethylaminoethyl ester of 3-nitroazulene-1-carboxylic acid, ethyl ester of 3-aminoazulene-1-carboxylic acid, and 2-diethylaminoethyl ester of 3-aminoazulene-1-carboxylic acid.—TULLY J. SPEAKER, *University of Connecticut School of Pharmacy*, and GLENDEN D. REDMAN, *Creighton University School of Pharmacy*. This investigation was supported in part by Public Health Service grant No. RG 7885.